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Nonallergic rhinitis: Common problem, chronic symptoms

ABSTRACT

Nonallergic rhinitis can significantly affect a patient's quality of life. It is difficult to distinguish from allergic rhinitis, but it has different triggers, and its response to treatment can vary. We review its differential diagnosis, causes, and treatment.

KEY POINTS

When evaluating a patient with rhinitis, a key question is whether it is allergic or nonallergic.

Identifying triggers that should be avoided is important for controlling symptoms.

If symptoms continue, then the first-line treatment for nonallergic rhinitis is intranasal steroids.

Failure of intranasal steroids to control symptoms should prompt a consideration of the many potential causes of rhinitis, and further evaluation and treatment can be tailored accordingly.

A 55-YEAR-OLD WOMAN has come to the clinic because of clear rhinorrhea and nasal congestion, which occur year-round but are worse in the winter. She reports that at times her nose runs continuously. Nasal symptoms have been present for 4 to 5 years but are worsening. The clear discharge is not associated with sneezing or itching. Though she lives with a cat, her symptoms are not exacerbated by close contact with it.

One year ago, an allergist performed skin testing but found no evidence of allergies as a cause of her rhinitis. A short course of intranasal steroids did not seem to improve her nasal symptoms.

The patient also has hypertension, hypothyroidism, and hot flashes due to menopause; these conditions are well controlled with lisinopril (Zestril), levothyroxine (Synthroid), and estrogen replacement. She has no history of asthma and has had no allergies to drugs, including nonsteroidal anti-inflammatory drugs (NSAIDs.)

How should this patient be evaluated and treated?

COMMON, OFTEN OVERLOOKED

Many patients suffer from rhinitis, but this problem can be overshadowed by other chronic diseases seen in a medical clinic, especially during a brief office visit. When a patient presents with rhinitis, a key question is whether it is allergic or nonallergic.

This review will discuss the different forms of nonallergic rhinitis and their causes, and give recommendations about therapy.

■ RHINITIS: ALLERGIC OR NONALLERGIC?

While allergic rhinitis affects 30 and 60 million Americans annually, or between 10% to 30% of US adults,¹ how many have nonallergic rhinitis has been difficult to determine.

In a study in allergy clinics, 23% of patients with rhinitis had the nonallergic form, 43% had the allergic form, and 34% had both forms (mixed rhinitis).² Other studies have suggested that up to 52% of patients presenting to allergy clinics with rhinitis have nonallergic rhinitis.³

Over time, patients may not stay in the same category. One study found that 24% of patients originally diagnosed with nonallergic rhinitis developed positive allergy tests when retested 3 or more years after their initial evaluation.⁴

Regardless of the type, untreated or uncontrolled symptoms of rhinitis can significantly affect the quality of life.

All forms of rhinitis are characterized by one or more of the following symptoms: nasal congestion, clear rhinorrhea, sneezing, and itching. These symptoms can be episodic or chronic and can range from mild to debilitating. In addition, rhinitis can lead to systemic symptoms of fatigue, headache, sleep disturbance, and cognitive impairment and can be associated with respiratory symptoms such as sinusitis and asthma.¹

Mechanisms are mostly unknown

While allergic rhinitis leads to symptoms when airborne allergens bind with specific immunoglobulin E (IgE) in the nose, the etiology of most forms of nonallergic rhinitis is unknown. However, several mechanisms have been proposed. These include entopy (local nasal IgE synthesis with negative skin tests),⁵ nociceptive dysfunction (hyperactive sensory receptors),⁶ and autonomic nervous system abnormalities (hypoactive or hyperactive dysfunction of sympathetic or parasympathetic nerves in the nose).⁷

Does this patient have an allergic cause of rhinitis?

When considering a patient with rhinitis, the most important question is, “Does this patient have an allergic cause of rhinitis?” Allergic

and nonallergic rhinitis have similar symptoms, making them difficult to distinguish. However, their mechanisms and treatment differ. By categorizing a patient’s type of rhinitis, the physician can make specific recommendations for avoidance and can initiate treatment with the most appropriate therapy. Misclassification can lead to treatment failure, multiple visits, poor adherence, and frustration for patients with uncontrolled symptoms.

Patients for whom an allergic cause cannot be found by allergy skin testing or serum specific IgE immunoassay (ImmunoCap/RAST) for environmental aeroallergens are classified as having nonallergic rhinitis.

■ CLUES POINTING TO NONALLERGIC VS ALLERGIC RHINITIS

Nonallergic rhinitis encompasses a range of syndromes with overlapping symptoms. While tools such as the Rhinitis Diagnostic Worksheet are available to help differentiate allergic from nonallergic rhinitis, debate continues about whether it is necessary to characterize different forms of rhinitis before initiating treatment.⁸

The diagnosis of nonallergic rhinitis depends on a thorough history and physical examination. Key questions relate to the triggers that bring on the rhinitis, which will assist the clinician in determining which subtype of rhinitis a patient may be experiencing and therefore how to manage it. Clues:

- Patients with nonallergic rhinitis more often report nasal congestion and rhinorrhea, rather than sneezing and itching, which are predominant symptoms of allergic rhinitis.
- Patients with nonallergic rhinitis tend to develop symptoms at a later age.
- Common triggers of nonallergic rhinitis are changes in weather and temperature, food, perfumes, odors, smoke, and fumes. Animal exposure does not lead to symptoms.
- Patients with nonallergic rhinitis have few complaints of concomitant symptoms of allergic conjunctivitis (itching, watering, redness, and swelling).
- Many patients with nonallergic rhinitis find that antihistamines have no benefit.

One-fourth to one-half of patients with chronic rhinitis may have the nonallergic form

Also, they do not have other atopic diseases such as eczema or food allergies and have no family history of atopy.

PHYSICAL FINDINGS

Some findings on physical examination may help distinguish allergic from nonallergic rhinitis.

- Patients with long-standing allergic rhinitis may have an “allergic crease,” ie, a horizontal wrinkle near the tip of the nose caused by frequent upward wiping. Another sign may be a gothic arch, which is a narrowing of the hard palate occurring as a child.
- In allergic rhinitis, the turbinates are often pale, moist, and boggy with a bluish tinge.
- Findings such as a deviated nasal septum, discolored nasal discharge, atrophic nasal mucosa, or nasal polyps should prompt consideration of the several subtypes of nonallergic rhinitis (TABLE 1).

CASE CONTINUED

Our patient's symptoms can be caused by many different factors. Allergic triggers for rhinitis include both indoor and outdoor sources. The most common allergens include cat, dog, dust mite, cockroach, mold, and pollen allergens. The absence of acute sneezing and itching when around her cat and her recent negative skin-prick tests confirm that the rhinitis symptoms are not allergic.

In this patient, who has symptoms throughout the year but no allergic triggers, consideration of the different subtypes of nonallergic rhinitis may help guide further therapy.

SUBTYPES OF NONALLERGIC RHINITIS

Vasomotor rhinitis

Vasomotor rhinitis is thought to be caused by a variety of neural and vascular triggers, often without an inflammatory cause. These triggers lead to symptoms involving nasal congestion and clear rhinorrhea more than sneezing and itching. The symptoms can be sporadic, with acute onset in relation to identifiable nonallergic triggers, or chronic, with no clear trigger.

Gustatory rhinitis, for example, is a form of vasomotor rhinitis in which clear rhinor-

TABLE 1

Types of nonallergic rhinitis

Vasomotor rhinitis

Irritant-sensitive
Weather-sensitive, temperature-sensitive
Gustatory rhinitis

Drug-induced rhinitis

Aspirin, nonsteroidal anti-inflammatory drugs
Alpha receptor agonists and antagonists
Vasodilators
Antihypertensive drugs, other cardiovascular drugs
Oral contraceptives
Rhinitis medicamentosa

Infectious rhinitis

Acute upper respiratory tract infection
Chronic rhinosinusitis

Nonallergic rhinitis eosinophilic syndrome

Immunologic causes

Wegener granulomatosis
Sarcoidosis
Relapsing polychondritis
Midline granulomas
Churg-Strauss syndrome
Amyloidosis
Granulomatous infections

Occupational rhinitis

Hormonal rhinitis

Pregnancy
Menstruation
Hypothyroidism

Structural

Polyps
Deviated septum
Adenoidal hypertrophy
Tumors
Cerebrospinal fluid leak

Atrophic rhinitis

Infectious
Secondary

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Uncontrolled
rhinitis can
significantly
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rhea occurs suddenly while eating or while drinking alcohol. It may be prevented by using nasal ipratropium (Atrovent) before meals.

Irritant-sensitive vasomotor rhinitis. In some patients, acute vasomotor rhinitis symptoms are brought on by strong odors, cigarette smoke, air pollution, or perfume. When asked, most patients easily identify which of these irritant triggers cause symptoms.

Weather- or temperature-sensitive vasomotor rhinitis. In other patients, a change in temperature, humidity, or barometric pressure or exposure to cold or dry air can cause nasal symptoms.⁹ These triggers are often hard to identify. Weather- or temperature-sensitive vasomotor rhinitis is often mistaken for seasonal allergic rhinitis because weather changes occur in close relation to the peak allergy seasons in the spring and fall. However, this subtype does not respond as well to intranasal steroids.⁹

Other nonallergic triggers of vasomotor rhinitis may include exercise, emotion, and sexual arousal (honeymoon rhinitis).¹⁰

Some triggers, such as tobacco smoke and perfume, are easy to avoid. Other triggers, such as weather changes, are unavoidable. If avoidance measures fail or are inadequate, medications (described below) can be used for prophylaxis and symptomatic treatment.

Drug-induced rhinitis

Drugs of various classes are known to cause either acute or chronic rhinitis. Drug-induced rhinitis has been divided into different types based on the mechanism involved.¹¹

The local inflammatory type occurs in aspirin-exacerbated respiratory disease, which is characterized by nasal polyposis with chronic rhinosinusitis, hyposmia, and moderate to severe persistent asthma. Aspirin and other NSAIDs induce an acute local inflammation, leading to severe rhinitis and asthma symptoms. Avoiding all NSAID products is recommended; aspirin desensitization may lead to improvement in rhinosinusitis and asthma control.

The neurogenic type of drug-induced rhinitis can occur with sympatholytic drugs such as alpha receptor agonists (eg, clonidine [Catapres]) and antagonists (eg, prazosin [Minipress]).¹¹ Vasodilators, including phosphodies-

terase-5 inhibitors such as sildenafil (Viagra), can lead to acute rhinitis symptoms ("anniversary rhinitis").

Unknown mechanisms. Many other medications can lead to rhinitis by unknown mechanisms, usually with normal findings on physical examination. These include beta-blockers, angiotensin-converting enzyme inhibitors, calcium channel blockers, exogenous estrogens, oral contraceptives, antipsychotics, and gabapentin (Neurontin).

Correlating the initiation of a drug with the onset of rhinitis can help identify offending medications. Stopping the suspected medication, if feasible, is the first-line treatment.

Rhinitis medicamentosa, typically caused by overuse of over-the-counter topical nasal decongestants, is also classified under drug-induced rhinitis. Patients may not think of nasal decongestants as medications, and the physician may need to ask specifically about their use.

On examination, the nasal mucosa appears beefy red without mucous. Once a diagnosis is made, the physician should identify and treat the original etiology of the nasal congestion that led the patient to self-treat.

Patients with rhinitis medicamentosa often have difficulty discontinuing use of topical decongestants. They should be educated that the withdrawal symptoms can be severe and that more than one attempt at quitting may be needed. To break the cycle of rebound congestion, topical intranasal steroids should be used, though 5 to 7 days of oral steroids may be necessary.¹

Cocaine is a potent vasoconstrictor. Its illicit use should be suspected, especially if the patient presents with symptoms of chronic irritation such as frequent nosebleeds, crusting, and scabbing.¹²

Infectious rhinitis

One of the most common causes of acute rhinitis is upper respiratory infection.

Acute viral upper respiratory infection often presents with thick nasal discharge, sneezing, and nasal obstruction that usually clears in 7 to 10 days but can last up to 3 weeks. Acute bacterial sinusitis can follow, typically in fewer than 2% of patients, with symptoms of persistent nasal congestion, discolored mucus, facial pain, cough, and sometimes fever.

In nonallergic rhinitis, there is more nasal congestion and rhinorrhea; in allergic rhinitis, more sneezing and itching

Chronic rhinosinusitis is a syndrome with sinus mucosal inflammation with multiple causes. It is clinically defined as persistent nasal and sinus symptoms lasting longer than 12 weeks and confirmed with computed tomography (CT).¹³ The CT findings of chronic rhinosinusitis include thickening of the lining of the sinus cavities or complete opacification of the pneumatized sinuses.

Major symptoms to consider for diagnosis include facial pain, congestion, obstruction, purulent discharge on examination, and changes in olfaction. Minor symptoms are cough, fatigue, headache, halitosis, fever, ear symptoms, and dental pain.

Treatment may involve 3 or more weeks of an oral antibiotic and a short course of an oral steroid, a daily nasal steroid spray, or both oral and nasal steroids. Most patients can be managed in the primary care setting, but they can be referred to an ear, nose, and throat specialist, an allergist, or an immunologist if their symptoms do not respond to initial therapy.

Nonallergic rhinitis eosinophilic syndrome

Patients with nonallergic rhinitis eosinophilic syndrome (NARES) are typically middle-aged and have perennial symptoms of sneezing, itching, and rhinorrhea with intermittent exacerbations. They occasionally have associated hyposmia (impaired sense of smell).¹ The diagnosis is made when eosinophils account for more than 5% of cells on a nasal smear and allergy testing is negative.

Patients may develop nasal polyposis and aspirin sensitivity.¹ Entopy has been described in some.¹⁴

Because of the eosinophilic inflammation, this form of nonallergic rhinitis responds well to intranasal steroids.

Immunologic causes

Systemic diseases can affect the nose and cause variable nasal symptoms that can be mistaken for rhinitis. Wegener granulomatosis, sarcoidosis, relapsing polychondritis, midline granulomas, Churg-Strauss syndrome, and amyloidosis can all affect the structures in the nose even before manifesting systemic symptoms. Granulomatous infections in the nose may lead to crusting, bleeding, and nasal obstruction.¹

A lack of a response to intranasal steroids or oral antibiotics should lead to consideration of these conditions, and treatment should be tailored to the specific disease.

Occupational rhinitis

Occupational exposure to chemicals, biologic aerosols, flour, and latex can lead to rhinitis, typically through an inflammatory mechanism. Many patients present with associated occupational asthma. The symptoms improve when the patient is away from work and worsen throughout the work week.

Avoiding the triggering agent is necessary to treat these symptoms.

Hormonal rhinitis

Hormonal rhinitis, ie, rhinitis related to metabolic and endocrine conditions, is most commonly associated with high estrogen states. Nasal congestion has been reported with pregnancy, menses, menarche, and the use of oral contraceptives.¹⁵ The mechanism for congestion in these conditions still needs clarification.

When considering drug therapy, only intranasal budesonide (Rhinocort) has a pregnancy category B rating.

While hypothyroidism and acromegaly have been mentioned in reviews of nonallergic rhinitis, evidence that these disorders cause nonallergic rhinitis is not strong.^{16,17}

Structurally related rhinitis

Anatomic abnormalities that can cause persistent nasal congestion include nasal septal deviation, turbinate hypertrophy, enlarged adenoids, tumors, and foreign bodies. These can be visualized by simple anterior nasal examination, nasal endoscopy, or radiologic studies. If structural causes lead to impaired quality of life or chronic rhinosinusitis, then consider referral to a specialist for possible surgical treatment.

Clear spontaneous rhinorrhea, with or without trauma, can be caused by cerebrospinal fluid leaking into the nasal cavity.¹⁸ A salty, metallic taste in the mouth can be a clue that the fluid is cerebrospinal fluid. A definitive diagnosis of cerebrospinal fluid leak is made by finding beta-2-transferrin in nasal secretions.

Weather- or temperature-sensitive vasomotor rhinitis is frequently mistaken for seasonal allergic rhinitis

Our guidelines for treating nonallergic rhinitis

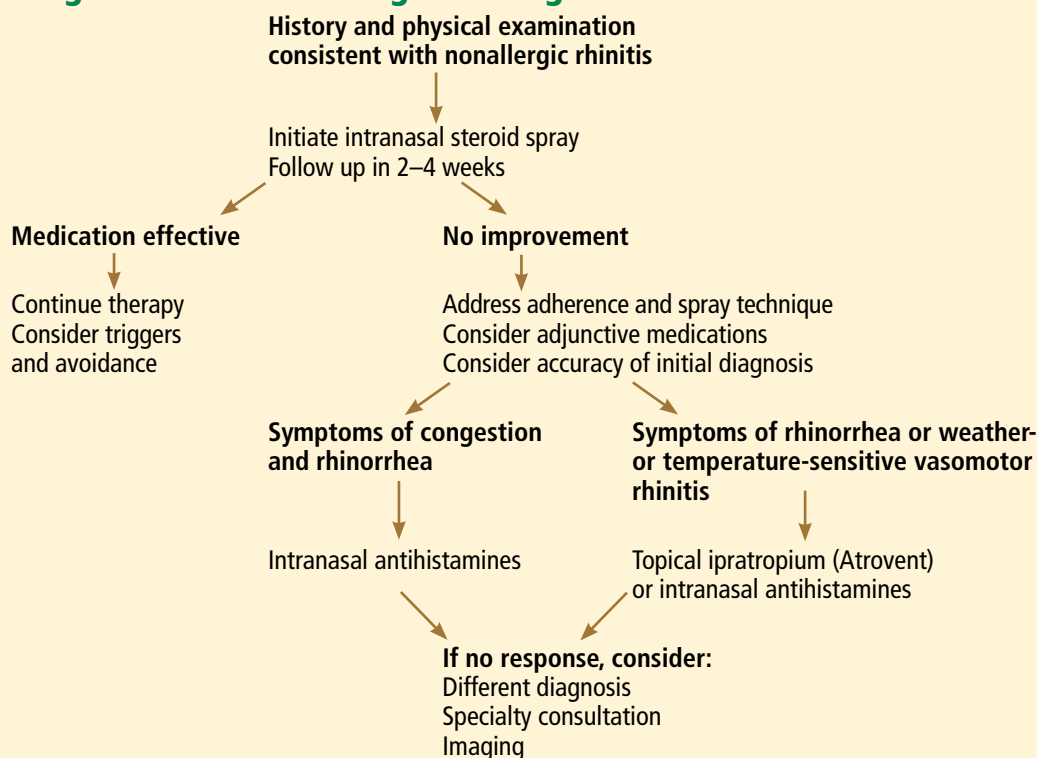


FIGURE 1

Suspect cocaine abuse if the patient presents with frequent nosebleeds, crusting, and scabbing

Atrophic rhinitis

Atrophic rhinitis is categorized as primary or secondary.

Primary (idiopathic) atrophic rhinitis is characterized by atrophy of the nasal mucosa and mucosal colonization with *Klebsiella ozaenae* associated with a foul-smelling nasal discharge.^{19,20} This disorder has been primarily reported in young people who present with nasal obstruction, dryness, crusting, and epistaxis. They are from areas with warm climates, such as the Middle East, Southeast Asia, India, Africa, and the Mediterranean.

Secondary atrophic rhinitis can be a complication of nasal or sinus surgery, trauma, granulomatous disease, or exposure to radiation.²¹ This disorder is typically diagnosed with nasal endoscopy and treated with daily saline rinses with or without topical antibiotics.²¹

CASE CONTINUED

Questioned further, our patient says her symptoms are worse when her husband smokes, but that she continues to have congestion and

rhinorrhea when he is away on business trips. She notes that her symptoms are often worse on airplanes (dry air with an acute change in barometric pressure), with weather changes, and in cold, dry environments. Symptoms are not induced by eating.

We note that she started taking lisinopril 2 years ago and conjugated equine estrogens 8 years ago. Review of systems reveals no history of facial or head trauma, polyps, or hyposmia.

The rhinitis and congestion are bilateral, and she denies headaches, acid reflux, and conjunctivitis. She has a mild throat-clearing cough that she attributes to postnasal drip.

On physical examination, her blood pressure is 118/76 mm Hg and her pulse is 64. Her turbinates are congested with clear rhinorrhea. The rest of the examination is normal.

AVOID TRIGGERS, PRETREAT BEFORE EXPOSURE

While treatment for nonallergic rhinitis varies according to the cause, there are some general guidelines for therapy (FIGURE 1).

TABLE 2

Medications recommended for treating nonallergic rhinitis

MEDICATION CLASS	OFFICIAL INDICATION FOR NONALLERGIC RHINITIS; BENEFITS	DOSING REGIMEN	APPROXIMATE COST
Intranasal corticosteroids Beclomethasone (Beconase AQ, Vancenase) Budesonide (Rhinocort AQ) Ciclesonide (Omnaris) Fluticasone (Flonase, Veramyst, generic) Mometasone (Nasonex) Triamcinolone (Nasacort)	Beclomethasone and fluticasone dipropionate have US Food and Drug Administration (FDA) indication Benefits: relief of nasal congestion, rhinorrhea, sneezing, and itching	Two sprays in each nostril once daily Stop if there is nasal bleeding and consult with physician	Generic: \$60 ^a Name brand: \$86–\$145 ^a
Intranasal antihistamines Azelastine (Astelin, Astepro) Olopatadine (Patanase)	Only Astelin has FDA indication Benefits: improvement of rhinorrhea, nasal congestion, sneezing and itching.	Two sprays in each nostril twice a day as needed	Astelin: \$120 ^a Astepro: \$108 ^a Patanase: \$135 ^a
Intranasal anticholinergic Ipratropium bromide 0.03% (Atrovent 0.03%)	Has FDA indication Benefits: decreases rhinorrhea	Two sprays each nostril two to three times a day	Generic: \$38 Name brand 0.03%: \$101
Oral decongestants Pseudoephedrine (eg, Sudafed) Phenylephrine	No indication Benefits: May be helpful for acute rhinorrhea and congestion	Not recommended for regular use	Sudafed 60 mg, 100 tablets: \$10.13

^aMost intranasal corticosteroids contain 120 sprays per bottle, which is 60 doses; Astelin and Astepro have 200 sprays, and Patanase has 200.

People with known environmental, non-immunologic, and irritant triggers should be reminded to avoid these exposures if possible.

If triggers are unavoidable, patients can pretreat themselves with topical nasal sprays before exposure. For example, if symptoms occur while on airplanes, then intranasal steroids or antihistamine sprays should be used before getting on the plane.

Many drugs available

Fortunately, many effective drugs are available to treat nonallergic rhinitis. These have few adverse effects or drug interactions.

Intranasal steroid sprays are considered first-line therapy, as there are studies demonstrating effectiveness in nonallergic rhinitis.²² Intranasal fluticasone propionate (Flonase) and beclomethasone dipro-

pionate (Beconase AQ) are approved by the US Food and Drug Administration (FDA) for treating nonallergic rhinitis. Intranasal mometasone (Nasonex) is approved for treating nasal polyps.

Nasal steroid sprays are most effective if the dominant nasal symptom is congestion, but they have also shown benefit for rhinorrhea, sneezing, and itching.

Side effects of nasal steroid sprays include nasal irritation (dryness, burning, and stinging) and epistaxis, the latter occurring in 5% to 10% of patients.²³

Intranasal antihistamines include azelastine (Astelin, Astepro) and olopatadine (Patanase). They are particularly useful for treating sneezing, congestion, and rhinorrhea.²⁴ Astelin is the only intranasal antihistamine with FDA approval for nonallergic rhinitis.

Side effects of this drug class include bitter taste (with Astelin), sweet taste (with As-tepro), headache, and somnolence.

Oral antihistamines such as loratadine (Claritin), cetirizine (Zyrtec), and fexofenadine (Allegra) are now available over the counter, and many patients try them before seeking medical care. These drugs may be helpful for those bothered by sneezing. However, no study has demonstrated their effectiveness for nonallergic rhinitis.²⁵ First-generation antihistamines may help with rhinorrhea via their anticholinergic effects.

Ipratropium, an antimuscarinic agent, decreases secretions by inhibiting the nasal parasympathetic mucous glands. Intranasal ipratropium 0.03% (Atrovent 0.03%) should be considered first-line if the dominant symptom is rhinorrhea. Higher-dose ipratropium 0.06% is approved for rhinorrhea related to the common cold or allergic rhinitis. Because it is used topically, little is absorbed. Its major side effect is nasal dryness.

Decongestants, either oral or topical, can relieve the symptoms of congestion and rhinorrhea in nonallergic rhinitis. They should only be used short-term, as there is little evidence to support their chronic use.

Phenylpropanolamine, a decongestant previously found in over-the-counter cough medicines, was withdrawn from the market in 2000 owing to concern that the drug, especially when used for weight suppression, was linked to hemorrhagic stroke in young women.^{26,27} Other oral decongestants, ie, pseudoephedrine and phenylephrine, are still available, but there are no definitive guidelines for their use. Their side effects include tachycardia, increase in blood pressure, and insomnia.

Nasal saline irrigation has been used for centuries to treat rhinitis and sinusitis, despite limited evidence of benefit. A Cochrane review concluded that saline irrigation was well tolerated, had minor side effects, and could provide some relief of rhinosinusitis symptoms either as the sole therapeutic measure or as adjunctive treatment.²⁸ Hypertonic saline solutions, while possibly more effective than isotonic saline in improving mucociliary clearance, are not as well tolerated since they can cause nasal burning and irritation. Presumed

benefits of saline irrigation are clearance of nasal secretions, improvement of nasociliary function, and removal of irritants and pollen from the nose.

A strategy

Initial therapy (TABLE 2) should be based on the presentation. If the patient has a limited response to the therapy at follow-up in 2 to 4 weeks, the physician should consider using adjunctive medications, address patient adherence and technique, and reassess the accuracy of the initial diagnosis. At this point, one can consider referral to a specialist such as an allergist or otolaryngologist, especially if there are comorbid conditions such as asthma or polyps.

Imaging the sinuses with CT, which has replaced standard nasal radiography, may help if one is concerned about chronic rhinosinusitis, nasal polyps, or other anatomic condition that could contribute to persistent symptoms. Cost and radiation exposure should enter into the decision to obtain this study because a diagnosis based on the patient's report of symptoms may be equally accurate.^{29,30}

CASE CONTINUED

Our patient has a number of potential causes of her symptoms. Exposure to second-hand tobacco smoke at home and to the air in airplanes could be acute triggers. Weather and temperature changes could explain her chronic symptoms in the spring and fall. Use of an angiotensin-converting enzyme inhibitor (in her case, lisinopril) and estrogen replacement therapy may contribute to perennial symptoms, but the onset of her nonallergic rhinitis does not correlate with the use of these drugs. There are no symptoms to suggest chronic rhinosinusitis or anatomic causes of her symptoms.

This case is typical of vasomotor rhinitis of the weather- or temperature-sensitive type. This diagnosis may explain her lack of improvement with intranasal steroids, though adherence and spray technique should be assessed. At this point, we would recommend trying topical antihistamines daily when chronic symptoms are present or as needed for acute symptoms.

Sexual arousal can lead to 'honeymoon rhinitis,' and erectile dysfunction drugs can lead to 'anniversary rhinitis'

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